



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application No. : 10/729,527  
Applicant : Williams  
Filed : December 5, 2003  
Title : SOLUBLE RECOMBINANT BOTULINUM TOXINS HAVING A C-  
TERMINAL PORTION OF A HEAVY CHAIN, A N-TERMINAL  
PORTION OF A HEAVY CHAIN AND A LIGHT CHAIN  
  
TC/A.U. : 1600/1645  
Examiner : PORTNER, V.A.  
  
Docket No. : D2939-CIPCONDIV3

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**CERTIFICATE OF MAILING**

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the date indicated below.

Date: June 10, 2003  
By: Loret McGree

**SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT**

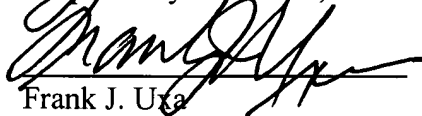
Dear Sir:

Applicant wishes to call to the attention of the Examiner the documents cited on the accompanying Form PTO-1449. The cited documents were either identified in one or more related applications or are applications related to the above-identified application. This communication is being submitted under 37 C.F.R. 1.97(c)(2). The Commissioner is hereby authorized to charge the necessary fee to Deposit Account No. 01-0885.

Each of these documents was cited in related (parent) application Serial No. 10/271,012 filed October 15, 2002. Therefore, no copies of these documents are submitted herewith. Applicant requests that each of these documents be made of record in the above-identified application.

Date: 6/10/05

Respectfully submitted,

  
Frank J. Uxa

Registration No. 25,612

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Form PTO-1449

# **INFORMATION DISCLOSURE CITATION IN AN APPLICATION**

(Use several sheets if necessary)

Docket No.: D2939-CIPCONDIV3

Application No.: 10/729,527

Applicant: Williams

Filing Date: December 5, 2003

Group Art Unit: 1645

## **U. S. PATENT DOCUMENTS**

| EXAMINER<br>INITIAL | DOCUMENT NUMBER | DATE    | NAME           | CLASS | SUBCLASS | FILING DATE<br>IF APPROPRIATE |
|---------------------|-----------------|---------|----------------|-------|----------|-------------------------------|
|                     | 5,071,759       | 12/1991 | Rothman et al. |       |          |                               |
|                     | 5,196,193       | 03/1993 | Carroll        |       |          |                               |
|                     | 5,268,295       | 12/1993 | Serrero        |       |          |                               |
|                     | 5,310,663       | 05/1994 | Dobeli et al.  |       |          |                               |
|                     | 5,410,019       | 04/1995 | Coy et al.     |       |          |                               |
|                     | 5,565,334       | 10/1996 | Kufe et al.    |       |          |                               |
|                     | 5,837,264       | 11/1998 | Becker et al.  |       |          |                               |
|                     | 5,837,265       | 11/1998 | Montal et al.  |       |          |                               |
|                     | 5,874,415       | 02/1999 | Kufe et al.    |       |          |                               |
|                     | 5,891,842       | 04/1999 | Kream          |       |          |                               |
|                     | 5,919,665       | 07/1999 | Williams       |       |          |                               |
|                     | 5,939,070       | 08/1999 | Johnson et al. |       |          |                               |

## **FOREIGN PATENT DOCUMENTS**

|  | DOCUMENT NUMBER | DATE    | COUNTRY | CLASS | SUBCLASS | TRANSLATION |    |
|--|-----------------|---------|---------|-------|----------|-------------|----|
|  |                 |         |         |       |          | YES         | NO |
|  | 93/05800        | 04/1993 | WO      |       |          |             |    |
|  | 94/13264        | 06/1994 | WO      |       |          |             |    |
|  | 94/21684        | 09/1994 | WO      |       |          |             |    |
|  | 95/32738        | 12/1995 | WO      |       |          |             |    |
|  | 96/05222        | 02/1996 | WO      |       |          |             |    |

## **OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)**

|    |  |
|----|--|
| AA | U.S. Application No. 08/704,159, filed 8/28/1996, Williams (Docket No. D2939-CIP)          |
| AB | U.S. Application No. 10/271,012, filed 10/15/2002, Williams (Docket No. D2939-CIPCON)      |
| AC | U.S. Application No. 10/728,696, filed 12/05/2003, Williams (Docket No. D2939-CIPCONDIV01) |
| AD | U.S. Application No. 10/729,122, filed 12/05/2003, Williams (Docket No. D2939-CIPCONDIV02) |
| AE | U.S. Application No. 10/729,039, filed 12/05/2003, Williams (Docket No. D2939-CIPCONDIV04) |
| AF | U.S. Application No. 11/001,241, filed 11/30/2004, Williams (Docket No. D2939-CIPCONCON)   |
| AG | U.S. Application No. 10/354,774 filed 01/30/2003, Williams (Docket No. D2939-CIPCON2)      |
| AH | U.S. Application No. 10/727,898, filed 12/04/2003, Williams (Docket No. D2939-CIPCON2DIV)  |

EXAMINER

DATE CONSIDERED

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|  |                 | Filing Date: December 5, 2003  |                 | Group Art Unit: 1645        |          |                               |    |
| <b>U. S. PATENT DOCUMENTS</b>  |                 |  |                 |                             |          |                               |    |
| EXAMINER<br>INITIAL  | DOCUMENT NUMBER | DATE   | NAME            | CLASS                       | SUBCLASS | FILING DATE<br>IF APPROPRIATE |    |
|  | 5,955,368       | 09/1999  | Johnson et al.  |                             |          |                               |    |
|  | 6,022,950       | 02/2000  | Murphy          |                             |          |                               |    |
|  | 6,287,566       | 09/2001  | Dertzbaugh      |                             |          |                               |    |
|  | 6,545,126       | 04/2003  | Johnson et al.  |                             |          |                               |    |
|  | 6,787,517       | 09/2004  | Gil et al.      |                             |          |                               |    |
| <b>FOREIGN PATENT DOCUMENTS</b>  |                 |  |                 |                             |          |                               |    |
|  | DOCUMENT NUMBER | DATE   | COUNTRY         | CLASS                       | SUBCLASS | TRANSLATION                   |    |
|  |                 |  |                 |                             |          | YES                           | NO |
|  | EP 0 209 281    | 01/1987  | Europe          |                             |          |                               |    |
|  | EP 0 282 042    | 09/1988  | Europe          |                             |          |                               |    |
|  | EP 0 593 176    | 04/1994  | Europe          |                             |          |                               |    |
|  | GB 2 272 697    | 05/1994  | Great Britain   |                             |          |                               |    |
|  |                 |  |                 |                             |          |                               |    |
| <b>OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)</b>  |                 |  |                 |                             |          |                               |    |
|  | AI              | Ford et al., (1991) Protein Expression & Purification, 2:95-107  |                 |                             |          |                               |    |
|  | AJ              | Kimura et al., (1991) Applied & Enviro Microbio, 57(4):1168-72   |                 |                             |          |                               |    |
|  | AK              | TaKaRa Shuzo Co. Catalog of TAKARA BIO INC at the web site: bio.takara.co.jp                                     |                 |                             |          |                               |    |
|  | AL              | Nassau et al., (1996) J. Bacterio, 178(4):1047-52  |                 |                             |          |                               |    |
|  | AM              | Hill et al., (1996) Arch. Biochem. and Biophys. 336(2):283-9.  |                 |                             |          |                               |    |
|  | AN              | Crowe et al., (1994) Methods in Molecular Biology, 31:371-387.   |                 |                             |          |                               |    |
|  | AO              | Maisey et al., (1988) Eur. J. Biochem 177:683-691  |                 |                             |          |                               |    |
|  | AP              | Rudinger, J. in Peptide Hormones, Parsons, J.A. (Ed,) Univ. Park Press, Baltimore, MD pp. 1-7.                   |                 |                             |          |                               |    |
|  | AQ              | Roitt, I. Essential Immun., 6 <sup>th</sup> Edition, Blackwell Scientific Publications, Boston, MA, pp. 173-178. |                 |                             |          |                               |    |
|  | AR              | LeClerc, C. et al. J. Immunol. 144(8): 3174-3182   |                 |                             |          |                               |    |
|  | AS              | Kleid, D.G. Annals NY Acad. Sci. 413:23-30.  |                 |                             |          |                               |    |
|  | AT              | Siegel, L.J. Clin. Microbiol. 26: 2351-2356.   |                 |                             |          |                               |    |
|  | AU              | Swiss-Prot Accession Number Q60393, Botulinum neurotoxin type G, Campbell, K et al (1993) cited therein.         |                 |                             |          |                               |    |
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| Form PTO-1449   |                 |   | Docket No.: D2939-CIPCONDIV3  |       | Application No.: 10/729,527 |                               |
| <b>INFORMATION DISCLOSURE CITATION<br/>IN AN APPLICATION</b><br><small>(Use several sheets if necessary)</small>  |                 |   | Applicant: Williams           |       |                             |                               |
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| EXAMINER<br>INITIAL   | DOCUMENT NUMBER | DATE  | NAME                          | CLASS | SUBCLASS                    | FILING DATE<br>IF APPROPRIATE |
|   | 2003/0049264    | 03/2003   | Foster et al.                 |       |                             |                               |
|   | 2003/0185850    | 10/2003   | Dertzbaugh                    |       |                             |                               |
|   | 5,601,823       | 02/1997   | Williams et al.               |       |                             |                               |
|   | 5,814,477       | 09/1998   | Williams et al.               |       |                             |                               |
|   | 6,573,244       | 06/2003   | Gordon et al.                 |       |                             |                               |
| <b>FOREIGN PATENT DOCUMENTS</b>   |                 |   |                               |       |                             |                               |
|   | DOCUMENT NUMBER | DATE  | COUNTRY                       | CLASS | SUBCLASS                    | TRANSLATION                   |
|   |                 |   |                               |       |                             | YES      NO                   |
|   |                 |   |                               |       |                             |                               |
| <b>OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)</b>   |                 |   |                               |       |                             |                               |
|   | AV              | Dertzbaugh, MT et al, Vaccine, Vol. 14(16), pages 1538-1544, 1996, Mapping of protective and cross-reactive domains of the type A neurotoxin of Clostridium botulinum.  |                               |       |                             |                               |
|   | AW              | Beitle et al., "One-step purification of a model periplasmic protein from inclusion bodies by its fusion to an effective metal-binding peptide", Biotechnology Progress, Vol. 9, pp 64-69 (1993).                 |                               |       |                             |                               |
|   | AX              | Kamiya et al., "Production of Monoclonal Antibody to Clostridium Difficile Toxin A Which Neutralizes Enterotoxicity But Not Haemagglutination Activity", FEMS Microbiology Letters, Vol. 81, pages 311-316 (1991) |                               |       |                             |                               |
|   | AY              | Hatheway, "Toxigenic Clostridia", Clin. Microbiology Reviews, Vol. 3, No. 1, pages 66-98 (1990)   |                               |       |                             |                               |
|   | AZ              | Coughlin et al., Characterization of six murine monoclonal antibodies specific for toxin B of Clostridium difficile", Hybridoma, Vol. 13, pages 147-152 (1994).   |                               |       |                             |                               |
|   | BA              | Hochuli et al., "Generic approach to facilitate purification of recombinant proteins with a novel metal chelate adsorbent", Biotechnology, Vol. 6, pages 1321-1325 (1988).  |                               |       |                             |                               |
|   | BB              | Lilius et al., "Metal affinity precipitation of proteins carrying genetically attached polyhistidine affinity tails", Eur. J. Biochem., Vol. 198, pages 499-504 (1991).   |                               |       |                             |                               |
|   | BC              | Wiedemann et al., "Chicken egg antibodies for prophylaxis and therapy of infectious intestinal diseases", J. Vet. Med., Vol. 38, pages 283-291 (1991).  |                               |       |                             |                               |
|   | BD              | Handl et al., High yield of active STb enterotoxin from a fusion protein (MBP-STb) expressed in E. Coli", Protein Expression and Purification, Vol. 4, pages 275-281 (1993).                                      |                               |       |                             |                               |
|   | BE              | Von Eichel-Streiber et al., "Cloning of Clostridium difficile toxin B gene and demonstration of high N-terminal homology between A and B", Med. Microbiol. Immunol., Vol. 179, pp 271-279 (1990).                 |                               |       |                             |                               |
|   | BF              | Kim et al, Characterization of protective antibodies in hamsters immunized against Clostridium difficile toxins A and B", Microbial Ecology in Health and Disease, Vol. 2, pp 47-59 (1989).                       |                               |       |                             |                               |
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|  | BG              | Zhou et al., "Expression and Purification of the Light Chain of Botulinum Neurotoxin A: A single mutation abolishes its Cleavage of SNAP-25 and Neurotoxicity after reconstruction with the Heavy Chain", Biochemistry, Vol. 34, No. 46, pages 15175-15181 (1995) |                        |                             |          |                               |
|  | BH              | Clayton et al, "Protective vaccination With a Recombinant Fragment of Clostridium Botulinum Neurotoxin Serotype A Expressed from a Synthetic Gene in E Coli", Infection and Immunity, Vol. 63, No. 7, pages 2738-2742 (1995).                                     |                        |                             |          |                               |
|  | BI              | Schiavo et al, "Tetanus and Botulinum-B Neurotoxins Block Neurotransmitter Release by Proteolytic Cleavage of Synaptobrevin", Nature, Vol. 359, pages 832-835 (1992)  |                        |                             |          |                               |
|  | BJ              | Kriegelstein et al., J. Protein Chem. 1994 Jan; 13(1):49-57.  |                        |                             |          |                               |
|  | BK              | Hutson et al., FEMS Microbiol Lett. 1993 Mar 15; 108(1):103-10.   |                        |                             |          |                               |
|  | BL              | Szabo et al., Appl Environ. Microbiol, 1993, 59(9):3011-3020.   |                        |                             |          |                               |
|  | BM              | Minton et al., "Host: Vector systems for gene cloning in Clostridium", Microbiological Sciences, 5(10):310-315 (1988).  |                        |                             |          |                               |
|  | BN              | Jung et al, "Cloning of a Clostridium botulinum type B toxin gene fragment encoding the N-terminus of the heavy chain", FEMS Microbiol. Lett., 70(1):69-72 (1992).  |                        |                             |          |                               |
|  | BO              | Campbell et al., "Gene Probes for Identification of the Botulinal Neurotoxin Gene and Specific Identification of Neurotoxin Types B, E, and F", Jour. Clin. Microbiology, Vol. 31, No. 9, pages 2255-2262 (1993).   |                        |                             |          |                               |
|  | BP              | Hauser et al., "Nucleotide sequence of Clostridium botulinum C1 neurotoxin", Nucleic Acids Research, Vol. 18, No. 16, page 4924 (1990).   |                        |                             |          |                               |
|  | BQ              | Mierendorf et al, "The pET System: Your choice for Expression", in Novations, Newsletter of Novagen, Inc., Vol. 1, No. 1, pp 1-3, May 1994.   |                        |                             |          |                               |
|  | BR              | Moberg et al., "Affinity Chromatography Purification of Type A Botulinum Neurotoxin from Crystalline Toxin Complex", Applied and Environ. Microbiology, Vol. 35, No. 5, pp 878-880 (1978).  |                        |                             |          |                               |
|  | BS              | Kimura K., English abstract: "The structure and function of botulinum type C neurotoxin", Hokkaido Igaku Zasshi [Article in Japanese], 1991 Nov; 66(6):841-8.   |                        |                             |          |                               |
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| <b>OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)</b>                     |                 |  |                               |       |                             |                               |
|   | BT              | Aktories, K et al, Biochem. J. 1987, October 15, vol. 247(2) pages 363-368 (abstract only)                             |                               |       |                             |                               |
|   | BU              | Valderrama, F. et al, PNAS, Vol. 97(4) pages 1560-1565, February 15, 2000  |                               |       |                             |                               |
|   | BW              | Poulain, B et al, Journal of Biological Chemistry, Vol. 264(36) issue of Dec. 25, pages 21928-21933, 1989.             |                               |       |                             |                               |
|   | BX              | Sathyamoorthy, Venugopal et al, The Journal of Biological Chemistry, vol. 260(19) pages 10461-10466, Sept. 5, 1985.    |                               |       |                             |                               |
|   | BY              | Pascchnik, VA et al, Bioseparation, Vol. 3, pages 267-283, 1993.   |                               |       |                             |                               |
|   | BZ              | DiBello, Cenci et al., European Journal of Biochemistry/FEBS (Germany) January 15, 1994, Vol. 219(1-2), pages 161-169. |                               |       |                             |                               |
|   | CA              | Niemann, H. et al, Behring. Inst. Mitt. No. 89, pages 153-162, 1991.   |                               |       |                             |                               |
|   | CB              | Fujii, N. et al, Appl. Environ. Microbiol., Jan. 1988, vol. 54(1), pages 69-73.  |                               |       |                             |                               |
|   | CC              | Syuto, B. et al, Journal of Biological Chemistry, vol. 256(8) April 25, 1981, pages 3712-3717.                         |                               |       |                             |                               |
|   | CD              | Young, M. et al, FEMS Microbiology Reviews, Vol. 63, pages 301-325, December 1989.                                     |                               |       |                             |                               |
|   | CE              | Kurazono (1992) Journal of Biological Chemistry, 267(21):14721-14729.  |                               |       |                             |                               |
|   | CF              | Mochida (1990) PNAS (USA), 87:7844-8.  |                               |       |                             |                               |
|   | CG              | Binz, T. et al., The Journal of Biological Chemistry, Vol. 266(16), pages 9153-9158, June 1990.                        |                               |       |                             |                               |
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